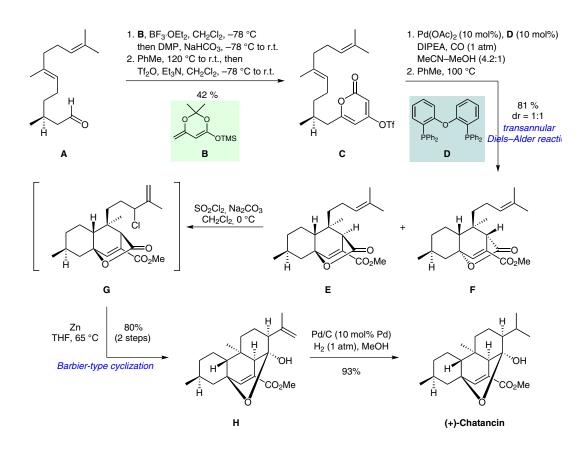
Synthesis of (+)-Chatancin

Short, Enantioselective Total Synthesis of Chatancin

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Significance: Platelet-activating factor (PAF) antagonist (+)-chatancin was isolated from the soft coral *Sarcophyton* species. Its unique carbon skeleton features a fused ring system bridged by a hemiketal, and six contiguous stereocenters. Biosynthetically, the natural product is hypothesized to originate from the macrocyclic diterpene cembrene A by a sequence of oxidations and a transannular Diels–Alder cycloaddition. Avoiding the lengthy synthesis of such a macrocycle, Zhao and Maimone employed a related Diels–Alder reaction prior to cyclizing the final ring. As a result, their route is remarkable for its conciseness, giving the natural product in only eight linear steps and 13% overall yield.

Comment: Starting from farnesal, a short sequence was devised to give key intermediate **C**. Quick access to pyrone **C** enabled the probing of the transannular Diels—Alder reaction as a means to construct the first decalin motif. Thus, palladium-catalyzed carbonylative esterification and subsequent heating in toluene gave diastereomers **E** and **F** exclusively, creating four new stereocenters in the process. Allylic chlorination yielded **G**, which was directly treated with zinc dust to give the full carbon skeleton as a single diastereomer in a Barbier-type annulation. After palladium-catalyzed regioselective hydrogenation of the *exo* olefin in **H**, (+)-chatancin was obtained. The structure was also confirmed by X-ray analysis.

SYNFACTS Contributors: Erick M. Carreira, Johannes Boshkow Synfacts 2015, 11(3), 0227 Published online: 16.02.2015 **DOI:** 10.1055/s-0034-1380006; **Reg-No.:** C00315SF